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**Proposed Claim Amendments
U.S.S.N. 10/729,581
Attorney Docket No. 23239-544**

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1. (currently amended) A method for identifying an aptamer that binds to a target molecule, wherein the aptamer comprises [[a]] 2'-OMe modified nucleotides, including at least one 2'-OMe GTP, comprising the following steps:

- a) preparing a transcription reaction mixture comprising (i) a modified RNA polymerase ~~that is able to incorporate any one of a 2'-OMe modified nucleotide triphosphate (2'-OMe NTP) selected from 2'-OMe ATP, 2'-OMe GTP, 2'-OMe CTP, 2'-OMe TTP and 2'-OMe UTP~~, wherein said modified RNA polymerase comprises at least one mutated amino acid residue as compared to the corresponding unmodified RNA polymerase, (ii) one or more 2'-OMe modified nucleotide triphosphates (2'-OMe NTPs), including at least one 2'-OMe GTP, (iii) 2'-OH guanosine triphosphate, (iv) magnesium ions, (v) manganese ions, wherein the concentration of magnesium ions is about 3 to 5 times greater than the concentration of manganese ions, and (vi) one or more double-stranded oligonucleotide transcription templates, wherein the modified RNA polymerase exhibits an increased ability to incorporate [[a]] 2'-OMe NTPs ~~modified nucleotide triphosphate (2'-modified NTP)~~ as compared to the ability of the corresponding unmodified RNA polymerase to incorporate the 2'-OMe NTPs;
- b) preparing a candidate mixture of single-stranded nucleic acids by transcribing the one or more oligonucleotide transcription templates under conditions whereby the modified RNA polymerase incorporates the 2'-OMe ~~modified NTPs~~, including at least one 2'-OMe GTP, into the nucleic acids of the said candidate mixture;
- c) contacting the candidate mixture with the said target molecule;
- d) partitioning the nucleic acids having an increased affinity to the target molecule relative to the nucleic acids ~~candidate mixture~~ from the remainder of the candidate mixture;
- e) amplifying the increased affinity nucleic acids, in vitro, using the transcription reaction mixture of step a) to generate a ligand-enriched mixture of nucleic acids

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of sufficient yield to repeat steps c), d) and e), whereby aptamers comprising at least one 2'-OMe GTP are identified; and
f) repeating steps c), d) and e) wherein the candidate mixture of step c) is the ligand-enriched mixture of nucleic acids from step e).

2 - 4. (cancelled)

5. (previously presented) The method of claim 1, wherein the modified RNA polymerase is a modified T7 RNA polymerase.

6. (previously presented) The method of claim 5, wherein the modified T7 RNA polymerase comprises a mutation at position 639 from a tyrosine residue to a phenylalanine residue (Y639F).

7. (previously presented) The method of claim 5, wherein the modified T7 RNA polymerase comprises a mutation at position 784 from a histidine residue to an alanine residue (H784A).

8. (previously presented) The method of claim 5, wherein the modified T7 RNA polymerase comprises a mutation at position 639 from a tyrosine residue to a phenylalanine residue and a mutation at position 784 from a histidine residue to an alanine residue (Y639F/H784A).

9. (currently amended) The method of claim 1, wherein the double-stranded oligonucleotide transcription template further comprises a leader sequence incorporated into a fixed region at the 5' end of the ~~oligonucleotide transcription~~ template.

10. (original) The method of claim 9, wherein the leader sequence comprises an all-purine leader sequence.

11. (currently amended) The method of claim 10, wherein the all-purine leader sequence has a length selected from the group consisting of at least 8 nucleotides long, at least 10 nucleotides long, at least 12 nucleotides long and at least 14 nucleotides long.

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12. (previously presented) The method of claim 1, wherein the transcription reaction mixture further comprises inorganic pyrophosphatase.

13. (cancelled)

14. (currently amended) The method of claim 1, wherein each NTP, 2'-modified NTP or 2'-OMe NTP is present at a concentration of about 0.5 mM, the concentration of magnesium ions is about 5.0 mM[[,]] and the concentration of manganese ions is about 1.5 mM.

15. (currently amended) The method of claim 1, wherein each NTP, 2'-modified NTP or 2'-OMe NTP is present at a concentration of about 1.0 mM, the concentration of magnesium ions is about 6.5 mM[[,]] and the concentration of manganese ions is about 2.0 mM.

16. (currently amended) The method of claim 1, wherein each NTP, 2'-modified NTP or 2'-OMe NTP is present at a concentration of about 2.0 mM, the concentration of magnesium ions is about 9.6 mM[[,]] and the concentration of manganese ions is about 2.9 mM.

17. (previously presented) The method of claim 1, wherein the transcription reaction mixture further comprises a substituted guanosine or guanosine.

18. (currently amended) The method of claim 17, wherein the ~~substituted guanosine or~~ guanosine is GMP.

19. (previously presented) The method of claim 1, wherein the transcription reaction mixture further comprises polyalkylene glycol.

20. (previously presented) The method of claim 19, wherein the polyalkylene glycol is polyethylene glycol.

21 - 76. (cancelled)

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77. (previously presented) The method of claim 1, wherein the 2'-OMe modified nucleotide triphosphates comprise a mixture of 2'-O-methyl adenosine triphosphate, 2'-O-methyl cytidine triphosphate, 2'-O-methyl uridine triphosphate or 2'-O-methyl thymidine triphosphate, 2'-O-methyl guanosine triphosphate and 2'-OH guanosine triphosphate, wherein the 2'-OH guanosine triphosphate comprises a maximum of about 10% of the total guanosine triphosphate population.

78. (currently amended) The method of claim 1, wherein the transcription reaction mixture further comprises spermidine, spermine, or both spermidine and spermine.

79. (currently amended) The method of claim 6 or claim 7, wherein the transcription reaction mixture further comprises inorganic pyrophosphatase.

80. (currently amended) The method of claim 130, wherein the ~~transcription mixture further comprises~~ guanosine is GMP.

81. (currently amended) The method of claim 80, wherein the oligonucleotide transcription template further comprises an all-purine leader sequence incorporated into a fixed region at the 5' end of the ~~oligonucleotide transcription~~ template.

82. (currently amended) The method of claim 81, wherein the all-purine leader sequence has a length selected from the group consisting of at least 8 nucleotides long_u[[;]] at least 10 nucleotides long_u[[;]] at least 12 nucleotides long[[;]] and at least 14 nucleotides long.

83. (currently amended) The method of claim 81, wherein the 2'-OMe~~ethyl~~ modified nucleotide triphosphates comprise a mixture of 2'-O-methyl adenosine triphosphate, 2'-O-methyl cytidine triphosphate, 2'-O-methyl uridine triphosphate or 2'-O-methyl thymidine triphosphate, 2'-O-methyl guanosine triphosphate[[,]] and 2'-OH guanosine triphosphate, wherein the 2'-OH guanosine triphosphate comprises a maximum of about 10% of the total guanosine triphosphate population.

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84. (currently amended) The method of claim 83, wherein the transcription reaction mixture further comprises spermidine, spermine, or both spermidine and spermine.

85. (currently amended) The method of claim 84, wherein the transcription reaction mixture further comprises polyethylene glycol.

86-87. (cancelled)

88. (currently amended) The method of claim 8 or 101, wherein the transcription reaction mixture further comprises inorganic pyrophosphatase.

89. (currently amended) The method of claim 131, wherein the ~~transcription mixture further~~ comprises guanosine is GMP.

90. (currently amended) The method of claim 89, wherein the oligonucleotide transcription template further comprises an all-purine leader sequence incorporated into a fixed region at the 5' end of the ~~oligonucleotide transcription~~ template.

91. (currently amended) The method of claim 90, wherein the all-purine leader sequence has a length selected from the group consisting of at least 8 nucleotides long, ~~at least 10 nucleotides long~~, at least 12 nucleotides long, and at least 14 nucleotides long.

92. (currently amended) The method of claim 91, wherein the 2'-O-Methyl modified nucleotide triphosphates comprise a mixture of 2'-O-methyl adenosine triphosphate, 2'-O-methyl cytidine triphosphate, 2'-O-methyl uridine triphosphate or 2'-O-methyl thymidine triphosphate, 2'-O-methyl guanosine triphosphate, and 2'-OH guanosine triphosphate, wherein the 2'-OH guanosine triphosphate comprises a maximum of about 10% of the total guanosine triphosphate population.

93. (currently amended) The method of claim 92, wherein the transcription reaction mixture further comprises spermidine, spermine, or both spermidine and spermine.

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94. (currently amended) The method of claim 93, wherein the transcription reaction mixture further comprises polyethylene glycol.

95 ~ 100. (cancelled)

101. (currently amended) A method for identifying an aptamer that binds to a target molecule, wherein the aptamer comprises [[a]] 2'-OMe modified nucleotides, including at least one 2'-OMe GTP, comprising the following steps:

- a) preparing a transcription reaction mixture comprising (i) a modified RNA polymerase that ~~is able to incorporate any one of a 2'-OMe modified nucleotide triphosphate (2'-OMe NTP) selected from 2'-OMe ATP, 2'-OMe GTP, 2'-OMe CTP, 2'-OMe TTP and 2'-OMe UTP~~, wherein said modified RNA polymerase comprises at least one mutated amino acid residue as compared to the corresponding unmodified RNA polymerase, (ii) one or more 2'-OMe modified nucleotide triphosphates (2'-OMe NTPs), including at least one 2'-OMe GTP, (iii) 2'-OH guanosine triphosphate, (iv) magnesium ions, (v) manganese ions, wherein the concentration of magnesium ions is about 3 to 5 times greater than the concentration of manganese ions, and (vi) one or more ~~partially double-stranded~~ oligonucleotide transcription templates, wherein the modified RNA polymerase exhibits an increased ability to incorporate [[a]] 2'-OMe NTPs modified nucleotide triphosphate (2'-modified NTP) as compared to the ability of the corresponding unmodified RNA polymerase to incorporate the 2'-OMe NTPs;
- b) preparing a candidate mixture of single-stranded nucleic acids by transcribing the one or more oligonucleotide transcription templates under conditions whereby the modified RNA polymerase incorporates the 2'-OMe ~~modified~~ NTPs, including at least one 2'-OMe GTP, into the nucleic acids of the ~~said~~ candidate mixture;
- c) contacting the candidate mixture with the ~~said~~ target molecule;
- d) partitioning the nucleic acids having an increased affinity to the target molecule relative to the nucleic acids ~~candidate mixture~~ from the remainder of the candidate mixture; and

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- e) amplifying the increased affinity nucleic acids, in vitro, using the transcription reation mixture of step a) to generate a ligand-enriched mixture of nucleic acids of sufficient yield to repeat steps c), d) and e), whereby aptamers comprising at least one 2'-OMe GTP are identified; and
- f) repeating steps c), d) and e) wherein the candidate mixture of step c) is the ligand-enriched mixture of nucleic acids from step e).

102. (currently amended) A method for transcribing an oligonucleotide[[,]] comprising the following steps:

- a) preparing a transcription reaction mixture comprising (i) a modified RNA polymerase that ~~is able to incorporate any one of a 2'-OMe modified nucleotide triphosphate (2'-OMe NTP) selected from 2'-OMe ATP, 2'-OMe GTP, 2'-OMe CTP, 2'-OMe TTP and 2'-OMe UTP, wherein said modified RNA polymerase~~ comprises at least one mutated amino acid residue as compared to the corresponding unmodified RNA polymerase, (ii) one or more 2'-OMe modified nucleotide triphosphates (2'-OMe NTPs), including at least one 2'-OMe GTP, (iii) 2'-OH guanosine triphosphate, (iv) magnesium ions, (v) manganese ions, wherein the concentration of magnesium ions is about 3 to 5 times greater than the concentration of manganese ions, and (vi) one or more double-stranded oligonucleotide transcription templates, wherein the modified RNA polymerase exhibits an increased ability to incorporate [[a]] 2'-OMe NTPs~~modified nucleotide triphosphate (2'-modified NTP)~~ as compared to the ability of the corresponding unmodified RNA polymerase to incorporate the 2'-OMe NTP; and
- b) transcribing the one or more oligonucleotide transcription templates under conditions to generate a transcribed oligonucleotide, whereby the modified RNA polymerase incorporates the 2'-OMe NTPs, including at least one 2'-OMe GTP, into the transcribed oligonucleotide.

103. (currently amended) The method of claim 102 or claim 182, wherein the modified RNA polymerase is a modified T7 RNA polymerase.

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104. (previously presented) The method of claim 103, wherein the modified T7 RNA polymerase comprises a mutation at position 639 from a tyrosine residue to a phenylalanine residue (Y639F).
105. (previously presented) The method of claim 103, wherein the modified T7 RNA polymerase comprises a mutation at position 784 from a histidine residue to an alanine residue (H784A).
106. (previously presented) The method of claim 103, wherein the modified T7 RNA polymerase comprises a mutation at position 639 from a tyrosine residue to a phenylalanine residue and a mutation at position 784 from a histidine residue to an alanine residue (Y639F/H784A).
107. (currently amended) The method of claim 102 or claim 182, wherein the double-stranded oligonucleotide transcription template further comprises a leader sequence incorporated into a fixed region at the 5' end of the ~~oligonucleotide-transcription~~ template.
108. (currently amended) The method of claim 107, wherein the leader sequence comprises is an all-purine leader sequence.
109. (currently amended) The method of claim 108, wherein the all-purine leader sequence has a length selected from the group consisting of at least 8 nucleotides long, at least 10 nucleotides long, ~~at least 12 nucleotides long~~ and at least 14 nucleotides long.
110. (currently amended) The method of claim 102 or claim 182, wherein the transcription reaction mixture further comprises a substituted guanosine or guanosine.
111. (currently amended) The method of claim 110, wherein the ~~substituted guanosine or~~ guanosine is GMP.

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112. (currently amended) The method of claim 102 or claim 182, wherein the transcription reaction mixture further comprises a polyalkylene glycol.
113. (previously presented) The method of claim 112, wherein the polyalkylene glycol is polyethylene glycol.
114. (currently amended) The method of claim 102 or claim 182, wherein the transcription reaction mixture further comprises inorganic pyrophosphatase.
115. (cancelled)
116. (currently amended) The method of claim 102 or claim 182, wherein each NTP, 2'-modified NTP or 2'-OMe NTP is present at a concentration of about 0.5 mM, the concentration of magnesium ions is about 5.0 mM[[,]] and the concentration of manganese ions is about 1.5 mM.
117. (currently amended) The method of claim 102 or claim 182, wherein each NTP, 2'-modified NTP or 2'-OMe NTP is present at a concentration of about 1.0 mM, the concentration of magnesium ions is about 6.5 mM[[,]] and the concentration of manganese ions is about 2.0 mM.
118. (currently amended) The method of claim 102 or claim 182, wherein each NTP, 2'-modified NTP or 2'-OMe NTP is present at a concentration of about 2.0 mM, the concentration of magnesium ions is about 9.6 mM[[,]] and the concentration of manganese ions is about 2.9 mM.
119. (currently amended) The method of claim 102 or claim 182, wherein the ~~one or more~~ 2'-modified nucleotide triphosphates comprise a mixture of 2'-O-methyl adenosine triphosphate, 2'-O-methyl cytidine triphosphate, 2'-O-methyl uridine triphosphate or 2'-O-methyl thymidine triphosphate, 2'-O-methyl guanosine triphosphate and 2'-OH guanosine triphosphate, wherein the 2'-OH guanosine triphosphate comprises a maximum of about 10% of the total guanosine triphosphate population.

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120. (currently amended) The method of any one of claims 104, 105 or 106, wherein the transcription reaction mixture further comprises inorganic pyrophosphatase.
121. (currently amended) The method of claim 132, wherein the ~~transcription mixture further comprises~~ guanosine is GMP.
122. (currently amended) The method of claim 121, wherein the double-stranded oligonucleotide transcription template further comprises a leader sequence incorporated into a fixed region at the 5' end of the ~~oligonucleotide transcription template~~.
123. (currently amended) The method of claim 122, wherein the leader sequence comprises ~~is~~ an all-purine leader sequence.
124. (currently amended) The method of claim 123, wherein the all-purine leader sequence has a length selected from the group consisting of at least 8 nucleotides long₁[[;]] at least 10 nucleotides long₂[[;]] at least 12 nucleotides long₃[[;]] and at least 14 nucleotides long.
125. (currently amended) The method of claim 123, wherein the 2'-OMe-~~methyl~~ modified nucleotide triphosphates comprise a mixture of 2'-O-methyl adenosine triphosphate, 2'-O-methyl cytidine triphosphate, 2'-O-methyl uridine triphosphate or 2'-O-methyl thymidine triphosphate, 2'-O-methyl guanosine triphosphate₁[[,]] and 2'-OH guanosine triphosphate, wherein the 2'-OH guanosine triphosphate comprises a maximum of about 10% of the total guanosine triphosphate population.
126. (currently amended) The method of claim 125, wherein the transcription reaction mixture further comprises spermidine, spermine, or both spermidine and spermine.
127. (currently amended) The method of claim 126, wherein the transcription reaction mixture further comprises polyethylene glycol.

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128-129. (cancelled)

130. (previously presented) The method of claim 79, wherein the transcription reaction mixture further comprises a substituted guanosine or guanosine.

131. (cancelled)

132. (previously presented) The method of claim 120, wherein the transcription reaction mixture further comprises a substituted guanosine or guanosine.

133. (new) The method of claim 1, wherein the concentration of magnesium ions is between 3.0 and 3.5 times greater than the concentration of manganese ions.

134. (new) The method of claim 101, wherein the modified RNA polymerase is a modified T7 RNA polymerase.

135. (new) The method of claim 134, wherein the modified T7 RNA polymerase comprises a mutation at position 639 from a tyrosine residue to a phenylalanine residue (Y639F).

136. (new) The method of claim 135, wherein the transcription reaction mixture further comprises inorganic pyrophosphatase.

137. (new) The method of claim 136, wherein the transcription reaction mixture further comprises a substituted guanosine or guanosine.

138. (new) The method of claim 137, wherein the guanosine is GMP.

139. (new) The method of claim 138, wherein the oligonucleotide transcription template further comprises an all-purine leader sequence incorporated into a fixed region at the 5' end of the template.

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140. (new) The method of claim 139, wherein the all-purine leader sequence has a length selected from the group consisting of at least 8 nucleotides long, at least 10 nucleotides long, at least 12 nucleotides long and at least 14 nucleotides long.

141. (new) The method of claim 139, wherein the 2'-OMe modified nucleotide triphosphates comprise a mixture of 2'-O-methyl adenosine triphosphate, 2'-O-methyl cytidine triphosphate, 2'-O-methyl uridine triphosphate or 2'-O-methyl thymidine triphosphate, 2'-O-methyl guanosine triphosphate and 2'-OH guanosine triphosphate, wherein the 2'-OH guanosine triphosphate comprises a maximum of about 10% of the total guanosine triphosphate population.

142. (new) The method of claim 141, wherein the transcription reaction mixture further comprises spermidine, spermine, or both spermidine and spermine.

143. (new) The method of claim 142, wherein the transcription reaction mixture further comprises polyethylene glycol.

144. (new) The method of claim 143, wherein the concentration of magnesium ions is between 3.0 and 3.5 times greater than the concentration of manganese ions.

145. (new) The method of claim 144, wherein the oligonucleotide transcription template is double-stranded.

146. (new) The method of claim 134, wherein the modified T7 RNA polymerase comprises a mutation at position 784 from a histidine residue to an alanine residue (H784A).

147. (new) The method of claim 146, wherein the transcription reaction mixture further comprises inorganic pyrophosphatase.

148. (new) The method of claim 147, wherein the transcription reaction mixture further comprises a substituted guanosine or guanosine.

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149. (new) The method of claim 148, wherein the guanosine is GMP.
150. (new) The method of claim 149, wherein the oligonucleotide transcription template further comprises an all-purine leader sequence incorporated into a fixed region at the 5' end of the template.
151. (new) The method of claim 150, wherein the all-purine leader sequence has a length selected from the group consisting of at least 8 nucleotides long, at least 10 nucleotides long, at least 12 nucleotides long and at least 14 nucleotides long.
152. (new) The method of claim 150, wherein the 2'-OMe modified nucleotide triphosphates comprise a mixture of 2'-O-methyl adenosine triphosphate, 2'-O-methyl cytidine triphosphate, 2'-O-methyl uridine triphosphate or 2'-O-methyl thymidine triphosphate, 2'-O-methyl guanosine triphosphate and 2'-OH guanosine triphosphate, wherein the 2'-OH guanosine triphosphate comprises a maximum of about 10% of the total guanosine triphosphate population.
153. (new) The method of claim 152, wherein the transcription reaction mixture further comprises spermidine, spermine, or both spermidine and spermine.
154. (new) The method of claim 153, wherein the transcription reaction mixture further comprises polyethylene glycol.
155. (new) The method of claim 154, wherein the concentration of magnesium ions is between 3.0 and 3.5 times greater than the concentration of manganese ions.
156. (new) The method of claim 155, wherein the oligonucleotide transcription template is double-stranded.
157. (new) The method of claim 134, wherein the modified T7 RNA polymerase comprises a mutation at position 639 from a tyrosine residue to a phenylalanine residue and a mutation at position 784 from a histidine residue to an alanine residue (Y639F/H784A).

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158. (new) The method of claim 157, wherein the transcription reaction mixture further comprises inorganic pyrophosphatase.
159. (new) The method of claim 158, wherein the transcription reaction mixture further comprises a substituted guanosine or guanosine.
160. (new) The method of claim 159, wherein the guanosine is GMP.
161. (new) The method of claim 160, wherein the oligonucleotide transcription template further comprises an all-purine leader sequence incorporated into a fixed region at the 5' end of the template.
162. (new) The method of claim 161, wherein the all-purine leader sequence has a length selected from the group consisting of at least 8 nucleotides long, at least 10 nucleotides long, at least 12 nucleotides long and at least 14 nucleotides long.
163. (new) The method of claim 162, wherein the 2'-OMe modified nucleotide triphosphates comprise a mixture of 2'-O-methyl adenosine triphosphate, 2'-O-methyl cytidine triphosphate, 2'-O-methyl uridine triphosphate or 2'-O-methyl thymidine triphosphate, 2'-O-methyl guanosine triphosphate and 2'-OH guanosine triphosphate, wherein the 2'-OH guanosine triphosphate comprises a maximum of about 10% of the total guanosine triphosphate population.
164. (new) The method of claim 163, wherein the transcription reaction mixture further comprises spermidine, spermine, or both spermidine and spermine.
165. (new) The method of claim 164, wherein the transcription reaction mixture further comprises polyethylene glycol.
166. (new) The method of claim 165, wherein the concentration of magnesium ions is between 3.0 and 3.5 times greater than the concentration of manganese ions.

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167. (new) The method of claim 166, wherein the oligonucleotide transcription template is double-stranded.
168. (new) The method of claim 101, wherein the oligonucleotide transcription template further comprises a leader sequence incorporated into a fixed region at the 5' end of the template.
169. (new) The method of claim 168, wherein the leader sequence comprises an all-purine leader sequence.
170. (new) The method of claim 169, wherein the all-purine leader sequence has a length selected from the group consisting of at least 8 nucleotides long, at least 10 nucleotides long, at least 12 nucleotides long and at least 14 nucleotides long.
171. (new) The method of claim 101, wherein each NTP, 2'-modified NTP or 2'-OMe NTP is present at a concentration of about 0.5 mM, the concentration of magnesium ions is about 5.0 mM and the concentration of manganese ions is about 1.5 mM.
172. (new) The method of claim 101, wherein each NTP, 2'-modified NTP or 2'-OMe NTP is present at a concentration of about 1.0 mM, the concentration of magnesium ions is about 6.5 mM and the concentration of manganese ions is about 2.0 mM.
173. (new) The method of claim 101, wherein each NTP, 2'-modified NTP or 2'-OMe NTP is present at a concentration of about 2.0 mM, the concentration of magnesium ions is about 9.6 mM and the concentration of manganese ions is about 2.9 mM.
174. (new) The method of claim 101, wherein the transcription reaction mixture further comprises a substituted guanosine or guanosine.
175. (new) The method of claim 174, wherein the guanosine is GMP.

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176. (new) The method of claim 101, wherein the transcription reaction mixture further comprises polyalkylene glycol.
177. (new) The method of claim 176, wherein the polyalkylene glycol is polyethylene glycol.
178. (new) The method of claim 101, wherein the 2'-OMe modified nucleotide triphosphates comprise a mixture of 2'-O-methyl adenosine triphosphate, 2'-O-methyl cytidine triphosphate, 2'-O-methyl uridine triphosphate or 2'-O-methyl thymidine triphosphate, 2'-O-methyl guanosine triphosphate and 2'-OH guanosine triphosphate, wherein the 2'-OH guanosine triphosphate comprises a maximum of about 10% of the total guanosine triphosphate population.
179. (new) The method of claim 101, wherein the transcription reaction mixture further comprises spermidine, spermine, or both spermidine and spermine.
180. (new) The method of claim 101, wherein the concentration of magnesium ions is between 3.0 and 3.5 times greater than the concentration of manganese ions.
181. (new) The method of claim 101, wherein the oligonucleotide transcription template is double-stranded.
182. (new) A method for transcribing an oligonucleotide comprising the steps:
- a) preparing a transcription reaction mixture comprising (i) a modified RNA polymerase that comprises at least one mutated amino acid residue as compared to the corresponding unmodified RNA polymerase, (ii) one or more 2'-OMe modified nucleotide triphosphates (2'-OMe NTPs), including at least one 2'-OMe GTP, (iii) 2'-OH guanosine triphosphate, (iv) magnesium ions, (v) manganese ions, wherein the concentration of magnesium ions is about 3 to 5 times greater than the concentration of manganese ions, and (vi) one or more oligonucleotide transcription templates, wherein the modified RNA polymerase exhibits an increased ability to incorporate 2'-OMe NTPs as compared to the ability of the corresponding unmodified RNA polymerase to incorporate the 2'-OMe NTP; and

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- b) transcribing the one or more oligonucleotide transcription templates under conditions to generate a transcribed oligonucleotide, whereby the modified RNA polymerase incorporates the 2'-OMe NTPs, including at least one 2'-OMe GTP, into the transcribed oligonucleotide.

183. (new) The method of claim 102 or 182, wherein the concentration of magnesium ions is between 3.0 and 3.5 times greater than the concentration of manganese ions.

184. (new) The method of claim 182, wherein the oligonucleotide transcription template is double stranded.

185. (new) The method of claim 127, wherein the concentration of magnesium ions is between 3.0 and 3.5 times greater than the concentration of manganese ions.

186. (new) The method of claim 185, wherein the oligonucleotide transcription template is double stranded.

187. (new) The method of claim 85, wherein the concentration of magnesium ions is between 3.0 and 3.5 times greater than the concentration of manganese ions.

188. (new) The method of claim 94, wherein the concentration of magnesium ions is between 3.0 and 3.5 times greater than the concentration of manganese ions.

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